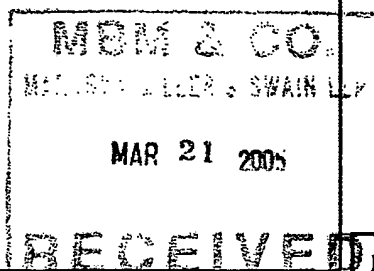


PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
MBM & CO.
P.O. Box 809
Station B
OTTAWA, Ontario
Canada, K1P 5P9



PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing 17 March 2005 (17-03-2005)
(day/month/year)

Applicant's or agent's file reference
831-156PCT

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/CA2004/001894

International filing date (day/month/year)
29 October 2004 (29-10-2004)

Priority date (day/month/year)
19 February 2004 (19-02-2004)

International Patent Classification (IPC) or both national classification and
IPC7 A61K-33/06; 9/68, 9/14; A61K-9/00; A61J-3/00

Applicant
VITALSTATE US INC. ET AL

1. This opinion contains indications relating to the following items :

- | | |
|--------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> Box No. I | Basis of the opinion |
| <input checked="" type="checkbox"/> Box No. II | Priority |
| <input type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Rule 43bis.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement. |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input checked="" type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
Place du Portage I, C114 - 1st Floor, Box PCT
50 Victoria Street
Gatineau, Quebec K1A 0C9

Authorized officer

Maja Solajic (819) 956-4121

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

**WRITTEN OPINION OF THE
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Box No. II

Priority

1. ☒ The following document has not yet been furnished :

☒ copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary :

**WRITTEN OPINION OF THE
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International application No.
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Box No. V **Reasoned statement under Rule 43bis.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	_____	YES
	Claims	1-34	NO
Inventive step (IS)	Claims	_____	YES
	Claims	1-34	NO
Industrial applicability (IA)	Claims	1-34	YES
	Claims	_____	NO

2. Citations and explanations :

The following relevant documents appear in the International Search Report:

D1: WO 03/088755 (Farber et al.)
D2: EP0966208 (Yang et al.)
D3: WO 01/76610 (Razus et al.)
D4: US 6,077,557 (Gordon et al.)
D5: US 5,928,664 (Yang et al.)
D7: GB 691,782 (Chivers and Sons Limited)
D6: US 4,597,981 (Kastin)
D8: Bell V. L. (Research Disclosure)
D9: DeMan "Principles of food chemistry"

Before assessing the novelty and inventiveness of the claimed subject matter it should be noted that present claims are directed to an extremely large number of possible compounds. These include: "sources of calcium", "hydrocolloids", "polyhydric alcohols", "sugar syrups", "modified starch" and "modified cellulose". Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is found, for only a small proportion of the claimed compounds. Consequently, the search has been limited and carried out for those compounds which are supported, disclosed in the description, examples and independent claims.

Furthermore, with respect to the moisture content, pH, and water activity of the calcium-based compositions, it is considered that a composition comprising calcium dispersed in a matrix (food, beverage, gel) which comprises propylene glycol, sugar solutions, starch, gellan gum, or gelatin would have a moisture content, pH, and water activity within the range provided in the instant claim set. Moreover, finding the optimum water activity would require only routine experimentation by one skilled in this art.

The subject matter of the present application relates to calcium gel delivery systems and the methods for making the same. Disclosed intermediate moisture, semi solid products are particularly useful for maintaining and improving bone density in a mammal. The systems comprise one or more sources of calcium which is uniformly dispersed in an ingestible matrix containing hydrocolloids, sugars and polyhydric alcohols. The delivery system may also comprise one or more other functional ingredients. The matrix of the delivery system provides for substantially uniform and complete dispersion of the calcium source (and other functional ingredients) and helps to minimise degradation of heat labile functional ingredients during manufacturing and storage. Disclosed manufacturing method comprises the steps of preparing a blend of hydrocolloids, sugars, or a combination thereof, and water; heating said blend to a temperature of less than 100°C; maintaining said blend at a temperature of less than 100°C; adjusting the moisture content of the blend to between about 10% and about 40% by weight; adding to said blend one or more functional ingredient [i.e. calcium] and a solvent component comprising one or more polyhydric alcohols at or below a temperature of 70°C to form a matrix whereby the one or more functional ingredient is substantially uniformly dispersed throughout said matrix, and moulding said matrix, wherein the delivery system has a final moisture content

(continued in Supplemental Box)

Box No. VII **Certain defects in the international application**

The following defects in the form or contents of the international application have been noted :

The following clerical errors are found in claims 15, 25, 26, 29 and 30:

- in claim 15, a period is missing; and
- in claims 25, 26, 29 and 30, the expression "said to calcium supplement" should probably read "said calcium supplement".

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 1, 17, 19 and dependent claims 3-5, 8, 13-15, 18, 20, 22-26, 28-30, 32 and 33 are indefinite and do not comply with Article 6 (PCT). The terms "one or more sources of calcium", "one or more hydrocolloids", "one or more polyhydric alcohols", "sugar syrups", "modified starch" and "modified cellulose" embrace a large number of different compounds and possibilities without clear qualification for solving the problem facing the inventor. [There is not sufficient information in the application by way of particular exemplification to establish that all above listed compounds have utility for applicant's purpose]. Therefore, the above claims lack support in description (Article 6 (PCT)). Furthermore, the definition "source of calcium" lacks clarity (Article 6 (PCT)).

Claims 19, 24, 28, 32 and 33 are indefinite in view of the usage of the terms/expressions:

- "optionally" claim 19, 32 and 33; and
- "in need thereof" claims 24 and 28.

A statement in an application, such as found on page 1, lines 7-8 and page 63, lines 19-23 which incorporates by reference any other document does not comply with Article 5 (PCT).

Additionally, the description does not meet the requirements of Article 5 (PCT), because it fails to fully identify a document on page 39, line 22-23, wherein a publication date is missing.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

between about 10% and about 40% and a water activity of less than about 0.7. Also disclosed are kits which comprise one or more packages containing delivery system in combination with a set of written instructions relating to their use.

D1 (Farber et al.) discloses oral delivery systems for functional ingredients and the method of making the same. The ingredients are selected from drugs, nutritional supplements, minerals [i.e. calcium], botanicals, and vitamins. As indicated in Table 1, proposed calcium gel delivery system is particularly useful in maintaining and improving bone health. Disclosed system is formulated as a foodstuff and comprises an ingestible matrix within which the functional ingredient(s) are substantially uniformly and completely dispersed and in which degradation of the functional ingredient(s) is minimised. The matrix comprises 1) a sugar component [i.e. one or more sugar, sugar syrup and/or sugar alcohol]; 2) one or more carbohydrate; 3) one or more hydrocolloid; 4) one or more polyhydric alcohol; 5) one or more source of mono- or divalent cations, and 5) water. Disclosed manufacturing method comprises the steps of preparing a blend of a carbohydrate, a hydrocolloid, a sugar, sugar alcohol or sugar syrup, or a combination thereof, and water; heating said blend to a temperature of less than 100°C; maintaining said blend at a temperature of less than 100°C; adjusting the moisture content of the blend to between about 15% and about 30% by weight; adding to said blend one or more functional ingredient [i.e. calcium] and a solvent component comprising one or more polyhydric alcohols at or below a temperature of 70°C to form a matrix whereby the one or more functional ingredient is substantially uniformly dispersed throughout said matrix, and moulding said matrix, wherein the delivery system has a final moisture content between about 15% and about 30% and a water activity of less than about 0.7. Also disclosed are dosage forms/kits with a set of written instructions relating to the use and dosage of functional ingredients.

References D2-D4 are representative of the prior art which relates to calcium fortified confectionary and gelled food products which have good taste, stability, texture and enhanced calcium bioavailability. Disclosed products are suitable for improving bone health in humans.

D2 (Young et al., EP '208) discloses fortified chewy confectionery products and methods of preparation thereof. Disclosed products are provided as delivery systems for minerals, such as calcium. The carbohydrates of the fortified confectionery products include at least one reducing sugar and one non-reducing sugar. The chewy confectionery products offer a matrix for about 0.2 wt. % to 45 wt. % of a fortifying component while maintaining a smooth and soft texture.

D3 (Razus et al.) relates to an oral formulation for calcium and the method of making the same. Disclosed formulation comprises calcium, a mixture of calcium and vitamin D, or mixture of calcium and magnesium with starch derivatives, mono and/or disaccharides, and xerogels [e.g. carrageenan]. The composition is in the form of powder, which after adding a liquid (i.e. water) and mixing, forms a pudding-like gelled suspension wherein the ingredients are dispersed homogeneously in a matrix. A reported clinical study showed excellent calcium bioavailability when compared with the standard preparation of effervescent tablets. The pharmaceutical composition is suitable for prevention and treatment of osteopenia and osteoporosis and is well tolerated by patients.

D4 (Gordon et al.) discloses intermediate moisture sweetened gelled food compositions fortified with calcium [i.e. calcium phosphate]. The gelled compositions comprise: A) carbohydrates [i.e. both monosaccharide and disaccharide sugars]; B) gelling agents [i.e. pectin]; C) calcium and about 2 to 20% moisture. Also disclosed are the preparation methods which involve the steps of: forming a calcium slurry which comprises calcium phosphate salts and propylene glycol and/or glycerine, forming a gellable blend, admixing the gellable composition with the slurry and forming into desired shaped and sized pieces.

References D5-D6 relate to methods of preparing consumable gellies and gummy delivery systems.

D5 (Yang et al, US '664) teaches a method of preparing a consumable gummy delivery system which comprises a gelatin matrix admixed with an active ingredient/agent [i.e. calcium carbonate and other mineral supplements]. Disclosed matrix is prepared by heating an aqueous solution of gelatin and glycerin to a temperature of from about 85 °C to below 100 °C in order to reduce a moisture content from about 10% to about 80% by weight of the matrix. A separate solution comprising an active

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of :

prepared by heating an aqueous solution of gelatin and glycerin to a temperature of from about 85 °C to below 100 °C in order to reduce a moisture content from about 10% to about 80% by weight of the matrix. A separate solution comprising an active agent or drug is prepared and admixed with the matrix composition. Other suitable ingredients such as: corn syrup, starches propylene glycol, various sweeteners and vitamins are also added. The matrix can be shaped into suitable shapes.

D6 (Chivers and Sons Ltd.) discloses a method for the manufacturing of tablet jellies which involves the steps of: (i) dispersing pectin and sucrose in water; (ii) heating the mixture at 82-93 °C; (iii) adding invert syrup and cane sugar to the mixture; (iv) concentrating the mixture to 75% soluble solids (15% water content); (v) adjusting the temperature to 82 °C (vi) mixing the dispersion with glycerol and (vii) forming droplets. The pH of the jelly is within the range of 2.8-5.5.

References D7-D8 are representative of the prior art which relates to confectionary products such as candies and marshmallows.

D7 (Kastin) discloses soft candy compositions which comprise, as principal ingredients, hydrogenated starch hydrolysate, sugars, sugar alcohols, dextrose, gelatin, water [6-20% by weight], flavourings and colourings.

D8 (Research Disclosure) describes formulations for marshmallows which comprise starch, gelatine, corn syrup, gellan gum, sugar, dextrose and water. The composition may also contain sorbitol.

D9 defines the general state of the art.

Novelty (Article 33(2) PCT)

Claims 1-34 do not meet the criteria of novelty because these claims include the subject matter disclosed in D1, as detailed above.

Claims 1, 3, 5-6, 8-11, 13, 15, 16-18, 24-31 do not meet the criteria of novelty because these claims include the subject matter disclosed in D2, as detailed above.

Claims 1, 5-6, 9-11, 16-17, 23, 24-31 do not meet the criteria of novelty because these claims include the subject matter disclosed in D3, as detailed above.

Claims 1, 5-7, 9-11, 16-17, 23-31 do not meet the criteria of novelty because these claims include the subject matter disclosed in D4, as detailed above.

Claims 19-22 do not meet the criteria of novelty because these claims include the subject matter disclosed in D5, as detailed above.

Inventive step (Art 33(3) PCT)

Claims 1-34 lack an inventive step under Article 33(3) PCT. More particularly:

Claims 1, 2, 4-11, 14, 17 and 23-31 lack an inventive step having regard to the combined teaching of D7-D8 and common general knowledge taken in the context of the state of the art. Although, D7 or D8 do not specifically teach the use of calcium in confectionary products it would be obvious to one of ordinary skill in this art to prepare a delivery system, comprising calcium dispersed in matrix (food, beverage, gel) which contains propylene glycol, sugar solutions, starch, gellan gum and gelatin as specified in D7 or D8. Since calcium supplementation is known for its benefits which include preventing bone disease, increasing bone density and improving bone health in mammals, it would be advantageous to supplement/fortify food [i.e. confectionary edible matrix] with calcium, which would be more beneficial to one's health than an ordinary unsupplemented food. Thus, it would be sufficient motivation for one of ordinary skill in the art to add calcium as an active/functional ingredient to the composition specified in D7 or D8, as noted above, because a calcium-based gel delivery system would be beneficial to one's bone health.

**WRITTEN OPINION OF THE
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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Claims 19-22 lack an inventive step having regard to the combined teaching of D6 and common general knowledge taken in the context of the state of the art. With regard to D6 document the method disclosed therein contains all the essential method steps as set forth in the instant claim 19, the only difference being calcium and the use of slightly lower temperature in the instant application [70°C; step iii)], while the temperature in D6 is 82°C. However, this is considered as a minor modification of the process in D6, which has no special advantage and which further leads to the same gel based product as disclosed in D6. Therefore, the selection of a lower temperature would be an obvious alternative for the skilled person in this art. With regard to calcium source it would be obvious to one of ordinary skill in the art to prepare a delivery system, comprising calcium dispersed in matrix (food, beverage, gel) which comprises propylene glycol, sugar solutions, starch, gellan gum and gelatin as specified in D6. Since calcium supplementation is known for its benefits which include preventing bone disease, increasing bone density and improving bone health in mammals, it would be advantageous to supplement/fortify food [i.e. confectionary edible matrix] with calcium, which would be more beneficial to one's health than an ordinary unsupplemented food. Thus, there is sufficient motivation for one of ordinary skill in the art to add calcium as an active/functional ingredient to the composition specified in D6, as noted above, because a calcium-based gel delivery system would be beneficial to one's bone health.

Having regard to claim 23, the International Searching and Preliminary Examining Authorities have divergent practices with respect to the search and examination of product by process claims. If the product in such a claim is the same as, or obvious from a product described in an item of prior art, the Canadian Intellectual Property Office for example considers the claim unpatentable even though the product described in the item of prior art was made by a different process.

Claims 32-34 are directed to kits comprising known components and therefore are considered to be non-inventive.

Industrial applicability (Article 33(4) PCT)

Claims 1-34 are industrially applicable and comply with Article 33(4) PCT.